General

Guideline Title

Clinical practice guideline on the management of invasive meningococcal disease.

Bibliographic Source(s)

Working Group of the Clinical Practice Guideline on the Management of Invasive Meningococcal Disease. Clinical practice guideline on the management of invasive meningococcal disease. Madrid (Spain): Ministry of Health, Social Services and Equality; Aragon Institute for Health Sciences; 2013. 173 p. (Clinical Practice Guidelines in the NHS: IACS; no. 2011/01). [134 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 12, 2016 – Fluoroquinolone Antibacterial Drugs : The U.S. Food and Drug Administration (FDA) is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

Recommendations

Major Recommendations

Levels of evidence (1++ to 4; 1a to 4) and grades of recommendation (A to D, Q, GCP) are defined at the end of the "Major Recommendations" field.

Diagnosis of Invasive Meningococcal Disease (IMD)

Warning Signs and Symptoms or Red Flag

Question to Answer

- In paediatric patients who come to primary health care (or emergency), what set of signs and symptoms should arouse suspicion of invasive meningococcal disease (IMD)?
    - Fever
    - Neck stiffness
    - Headache
    - Photophobia
    - Vomiting
    - Dizziness
    - Fast breathing
    - Drowsiness
    - Less than 50% of usual fluid intake in 24 hours (<1 year)
    - Strange pitched cry (<1 year)
    - Abnormal skin colour (pale, earthy, mottled, bluish)
    - Vascular collapse, hypotension, shock
    - Leg pain or refusal to walk
    - Rash
    - Changes in heart rate
    - Cold hands and feet

GCP - Health care professionals should be trained on how to recognize and manage IMD.

D - The presence of a generalized petechial or purpuric rash, with capillary refill >2 seconds in a paediatric patient with impairment of the general condition, should suggest IMD and the need for urgent treatment.

D - In the ill paediatric patient, the presence of any of the following signs and symptoms should alert the clinician about the possibility of IMD:

- Petechial rash (non-blanching)
- Capillary refill time >2 seconds
- Abnormal skin colour
- Decreased level of consciousness
- Pain in extremities
- Cold hands and feet
- Fever
- Headache
- Neck stiffness
- Photophobia

D - One must remain alert to the possibility of IMD when evaluating patients with acute febrile disease because in the first 4 to 6 hours of onset of the clinical IMD nonspecific symptoms such as fever, lethargy, refusal of food, nausea, vomiting, irritability, signs and/or symptoms of upper respiratory tract infection (runny nose, sore throat, etc.), diarrhoea, or abdominal pain may appear.

D - In the initial clinical evaluation (primary care), it should be noted that the following symptoms are very rare in the paediatric patient with mild febrile disease: leg pain, confusion, neck stiffness, and photophobia.

GCP - The clinician will take into account the fact that the signs and symptoms of the disease can vary and become more specific over time.

B - The set of clinical and laboratory findings which strongly suggest that the causal agent of bacterial meningitis is *Neisseria meningitidis* includes the presence of haemorrhagic rash + absence of seizures + headache + negative gram stain of cerebrospinal fluid (CSF).

Clinical Reassessment as Strategy to Improve Diagnosis

Questions to Answer

- For a paediatric patient who goes to primary health care with symptoms suggestive of IMD, does a second specific clinical evaluation (after 4 to 6 hours) for disease progression improve the diagnosis?
- For a paediatric patient who goes to primary health care with symptoms suggestive of IMD, does a telephone evaluation for disease

progression improve the diagnosis?

D - In the presence of clinical signs or other symptoms suggestive of IMD, treatment should not be delayed waiting for a second clinical evaluation.

GCP - Children with nonspecific symptoms at initial presentation, in whom IMD cannot be excluded at the discretion of the physician, should be reassessed in a short period of time (hours).

GCP - The health care professional will inform caregivers about the need to seek health care if the patient's condition deteriorates during childhood before the planned revaluation for example, if the characteristics of the rash change. The degree of concern of parents or caregivers as well as their ability to act if the patient worsens must be taken into account and information on the availability of health services in the area must be provided.

Non-specific Laboratory Tests

Question to Answer

- Among paediatric population with petechial rash, can non-specific laboratory tests (C-reactive protein [CRP], white cell count, blood gases), help to confirm or refute the diagnosis of IMD?

GCP - The following determinations should be performed in children with petechial rash of unknown origin and fever, or history of fever:

- Blood cell counts
- CRP or procalcitonin
- Coagulation tests
- Blood culture
- Blood glucose
- Pulse oximetry

C - If a paediatric patient has a petechial rash of unknown origin and fever, or history of fever, but none of the high-risk clinical features, the following recommendations should be considered:

- Start the specific treatment immediately if the CRP or the white cell count (especially neutrophil count) is high, since this indicates increased risk of IMD.
- Clinicians should be aware that although IMD is less likely with both normal CRP and white cell count, it should not be ruled out. Both parameters can be normal in severe or very short evolution cases.
- Evaluate clinical progression by monitoring vital signs, capillary refill time and oxygen saturation. Perform checks at least every hour for the next 4 to 6 hours.
- Treat with antibiotics and admit to hospital if doubt persists.

GCP - The serum procalcitonin concentration can be used as an early marker of IMD. Changes in the serum concentration of procalcitonin take place earlier and faster than those of the CRP.

GCP - If the final assessment is as being of low risk of IMD and the patient is discharged, it is recommended to warn caregivers to return if they feel that he/she worsens (for example, if new spots appear or if the patient seems excessively sleepy or irritable).

Diagnosis of Increased Intracranial Pressure

Question to Answer

- Among paediatric population with suspected or confirmed bacterial meningitis, can a cranial computed tomography (CT) reliably demonstrate an increase of intracranial pressure?

D - Clinical assessment, and not cranial CT, is recommended to decide whether it is safe to perform a lumbar puncture. CT is unreliable for identifying increased intracranial pressure.

D - If a CT has been performed, it is not recommended to do a lumbar puncture if there are radiological signs of increased intracranial pressure.

D - It is recommended not to delay the treatment while waiting for a CT to be performed.

Microbiological Confirmation Tests

Question to Answer

- In the case of patients with suspected IMD, what diagnostic tests done at an early stage are useful to confirm the diagnosis of IMD?
    - Blood culture
    - Skin scrapings
    - Blood polymerase chain reaction (PCR)
    - Throat swab
    - Urine rapid antigen testing
    - Blood rapid antigen testing

C - To confirm the diagnosis in patients with suspected IMD, blood should be drawn for bacterial culture.

D - To confirm the diagnosis in patients with suspected IMD, blood should be drawn to perform a meningococcal PCR (whole blood, ethylenediaminetetraacetic acid [EDTA]) in laboratories with sufficient technical capacity.

C - A lumbar puncture should be performed in patients with clinical features of meningitis without sepsis (purpura), if there are no contraindications.

D - The CSF should be referred to a microbiological laboratory. The following techniques should be performed:

- Microscopy
- Cultivation of bacteria
- Meningococcal PCR in laboratories with sufficient technical capacity

D - None of the following techniques is definitive when IMD is to be confirmed or ruled out: skin scraping, skin biopsy, petechial or purpuric lesion aspirates (obtained with a needle and syringe).

GCP - Samples should be collected as soon as possible after establishing the clinical suspicion and preferably before starting the antimicrobial treatment. The sample collection must not delay the onset of the antibiotic treatment.

Pre-hospital Management of IMD

Pre-hospital Administration of Antibiotics

Questions to Answer

- In patients with suspected IMD, does the pre-hospital administration of antibiotics reduce mortality?
- In patients with suspected IMD, does the pre-hospital administration of antibiotics affect morbidity and influence the admission to the intensive care unit (ICU), the duration of hospital stay, admission costs, the duration of school absence, etc.?
- In patients with suspected IMD who come to primary health care, does the parenteral administration of antibiotics reduce mortality and morbidity more than the oral administration of antibiotics?
- In patients with suspected IMD who come to primary health care, does the intramuscular administration of ceftriaxone have a similar efficacy and safety to its intravenous administration?

GCP - Patients with suspected IMD will be sent to hospital urgently.

D - When suspecting IMD, intravenous antibiotics (ceftriaxone 50 mg/kg IV or IM) should be administered as soon as possible, both in primary care and at a higher level, but the urgent transfer to hospital should not be delayed.

Pre-hospital Resuscitation

Question to Answer

- In patients with suspected IMD, does resuscitation before reaching the hospital (in the ambulance) improve survival? Can they reduce the severity of the disease and influence on the admission to the ICU, the duration of hospital stay, admission costs or the duration of school absence?

GCP - In patients with suspected or confirmed meningococcal sepsis, resuscitation should be started immediately, if possible, prior to initiating patient transport or during transport.

Development and Implementation of Protocols

Question to Answer

- Do care processes ("process mapping programs") for those patients with progressive symptoms improve survival or reduce the severity of the disease? Do these have any effect on the admission to the ICU or the duration of hospital stay, admission costs, the duration of school absence, etc.?

D - It is recommended to develop tools locally (clinical pathways, process maps, interdisciplinary agreements) to facilitate access and care of patients with IMD, taking into account the geography and the services available.

D - A periodic revision of the medical records of patients with IMD is recommended to identify avoidable situations and achieve optimal health care.

Hospital Management of IMD

Antibiotic Treatment

Questions to Answer

- What antibiotic regimen should be used to treat bacterial meningitis or confirmed meningococcal septicaemia?
- In patients with IMD, is a short treatment (≤7 days) as effective or more and as safe as or more to than a prolonged treatment (>7 days) to maintain or increase the cure rate of the disease and maintain or reduce the number of sequelae?

B - First-line antibiotics for the treatment of confirmed IMD are intravenous ceftriaxone every 12 hours for a total of 7 days, or cefotaxime, every 6 hours for a total of 7 days.

Sampling for Microbiological Diagnosis

Question to Answer

- In patients with suspected IMD treated at a hospital emergency unit, should the antibiotic treatment start immediately or should it start after the realization of the lumbar puncture and blood culture?

D - In a hospital emergency unit, when suspecting a case of IMD, obtaining samples from the patient for further confirmation of the diagnosis should not delay the beginning of the empirical antibiotic treatment.

GCP - Blood cultures should be performed as soon as possible, but should not delay treatment.

Indications for Lumbar Puncture in IMD

Questions to Answer

- In patients with suspected IMD, does lumbar puncture (early/late) affect the early/late onset of the specific treatment, the final diagnosis, as well as morbidity and mortality rates?
- Among paediatric population less than three months of age with bacterial meningitis, should a control lumbar puncture be done before stopping the antibiotic treatment?

GCP - Lumbar puncture is not recommended in the initial evaluation for suspected IMD with features of septicaemia. Late realization of the lumbar puncture may be considered if the diagnosis remains uncertain or there is inadequate clinical progression and no contraindications.

C - Lumbar puncture should be performed in patients with clinical meningitis without septicemic features (purpura) if there are no contraindications.

D - The CSF will be sent to the laboratory for microscopy, culture and PCR.

D - In paediatric patients who are clinically well and without evidence of bacterial disease, it is reasonable to observe the patient and defer the realization of the lumbar puncture.

GCP - It is advisable to repeat the lumbar puncture in paediatric patients aged between 1 and 3 months who have not been previously hospitalized in the following circumstances:

- Presence of persistent or recurrent fever
- Deterioration of the clinical condition
- New clinical findings (especially neurological) or persistently altered inflammatory reactants

GCP - It is not advisable to perform lumbar puncture to assess the success of treatment in paediatric patients aged between 1 and 3 months not

previously hospitalized in the following circumstances:

- In the case of patients receiving adequate antibiotic treatment against the causative agent, and whose clinical outcome is still good
- Before stopping antibiotic treatment if clinical response is good

Early Supportive Therapy

Question to Answer

- In patients with suspected IMD, do the following treatments reduce mortality and morbidity?
  - Corticosteroid therapy
  - Intravenous fluids to debate: colloid/crystalloid (Hartmann normal saline, Ringer's lactate), fresh frozen plasma (FFP), artificial colloids
  - Resuscitation (oxygen, airway care and circulatory system)

A - The adjuvant administration of a corticosteroid (dexamethasone intravenously at a dose of 0.15 mg/kg/dose up to 10 mg/dose, 4 times a day for 4 days) should be considered when there is a suspicion of bacterial meningitis or once it has been confirmed; it should be administered as soon as possible and it should not interfere with the administration of antibiotics and the transfer to a specialized centre.

B - Do not administer corticosteroids to paediatric patients with meningococcal septicaemia, except in cases of meningococcal septic shock resistant to catecholamine.

D - In patients with suspected or confirmed bacterial meningitis, the appearance of signs of shock, increased intracranial pressure and dehydration will be assessed.

D - The administration of fluids should not be restricted unless there is increased intracranial pressure or an increased secretion of antidiuretic hormone.

D - A volume of fluids should be administered and maintained to avoid hypoglycaemia and maintain the electrolyte balance.

D - Use enteral feeds as maintenance fluid if tolerated.

D - If it is necessary to maintain intravenous fluids, the use of isotonic fluids (0.9% sodium chloride with 5% glucose, or 0.9% sodium chloride with 5% dextrose) is recommended.

D - The administration of fluids and urine output should be monitored to ensure adequate hydration and prevent over-hydration.

D - Electrolytes and glucose should be monitored regularly (if intravenous liquids are administered at least once a day).

D - If there are signs of increased intracranial pressure or shock, it is recommended to start the emergency procedures relevant to these situations and discuss the management of fluids with a paediatric intensive care physician.

D - If there are signs of shock, give immediately 20 ml/kg of 0.9% sodium chloride in 5 to 10 minutes. Give the fluid intravenously or via an intraosseous route and reassess the patient immediately (see table, "Management of Paediatric Patients with IMD: Intravenous Fluid," below).

D - In self-ventilating children with suspected bacterial meningitis or confirmed meningococcal septicaemia, and signs of respiratory distress, the use of a facial mask is recommended to provide 15 litres of oxygen through a mask with reservoir (see table, "Management of Respiratory Support in Paediatric Patients with IMD," below). If there is a threat of loss of airway patency, airway opening manoeuvres should be applied; positive pressure ventilation through a mask ventilation bag and finally isolation of the airway.

Table: Management of Paediatric Patients with IMD: Intravenous Fluids

If there are signs of shock, an immediate fluid bolus of 20 ml/kg sodium chloride 0.9% in 5 to 10 minutes should be administered. Administer intravenously or via an intraosseous route and reassess the patient immediately afterwards. If the signs of shock persist, immediately administer a second bolus of 20 ml/kg of intravenous or intraosseous sodium chloride 0.9% or human albumin 4.5% solution in 5 to 10 minutes. If the signs of shock still persist after the first 40 ml/kg: • Immediately administer a third bolus of 20 ml/kg of intravenous or intraosseous sodium chloride 0.9% or human albumin 4.5% solution in 5 to 10 minutes.

- Call for anaesthetic assistance for urgent tracheal intubation and mechanical ventilation.
- Start treatment with vasoactive drugs.
- It must be noted that some patients may require large volumes of fluid over a short period of time to restore their circulating volume.
- Giving further fluid boluses at 20 ml/kg of intravenous or intraosseous sodium chloride 0.9% or human albumin 4.5% solution in 5 to 10 minutes should be considered, based on clinical signs and appropriate laboratory investigations including urea and electrolytes.

Discuss further management with a paediatric intensive care physician.

If shock persists despite fluid resuscitation (more than 40 ml/kg) and the treatment with either intravenous adrenaline or intravenous noradrenaline, or both, potential reasons (such as persistent acidosis, incorrect dilution, extravasation) should be considered and further management options should be discussed with a paediatric intensive care physician.

Use protocols for the administration of vasoactive agents in children and young people with suspected or confirmed bacterial meningitis or meningococcal septicaemia.

Table: Management of Respiratory Support in Paediatric Patients with IMD

A health care professional with expertise in paediatric airway management should undertake tracheal intubation.

It must be noted that children and young people with suspected or confirmed bacterial meningitis or meningococcal septicaemia are very ill and at grave risk of sudden deterioration during intubation. Anticipate aspiration, pulmonary oedema or worsening shock during intubation. Ensure that the patient is fasting from hospital admission and that the following elements are available before intubation:

- Facilities to administer fluid boluses
- Appropriate vasoactive drugs
- Access to a health care professional experienced in the management of critically ill paediatric patients

Tracheal intubation and mechanical ventilation should be undertaken for the following indications:

- Threatened (for example, loss of gag reflex), or actual loss of airway patency
- The need for any form of assisted ventilation
- Increased work of breathing
- Hypoventilation or apnoea
- Features of respiratory failure, including:
  - Irregular respiration (for example, Cheyne–Stokes breathing)
  - Hypoxia (partial pressure of arterial oxygen [PaO_2] less than 97.5 mmHg) or decreased oxygen saturations in air by pulsoximetry (O_2saturation <92%)
  - Hypercapnia ($PaCO_2$ greater than 45 mmHg)
- Continuing shock following infusion of a total of 40 ml/kg of resuscitation fluid
- Signs of raised intracranial pressure
- Impaired mental status:
  - Reduced or fluctuating level of consciousness (Glasgow Coma Scale score less than 9 or a drop of 3 or more)
  - Moribund state
- Control of intractable seizures
- Need for stabilization and management to allow brain imaging or transfer to the paediatric intensive care unit (ICU) of another hospital

Use local or national protocols for intubation.

Adapted from National Collaborating Centre for Women's and Children's Health, Commissioned by the National Institute for Health and Care Excellence (NICE). Bacterial meningitis and meningococcal septicaemia. Management of bacterial meningitis and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care. London: Royal College of Obstetricians and Gynaecologists; 2010.

Stabilization and Transportation to a Paediatric ICU

Question to Answer

- Do specialized transport teams improve outcomes and reduce adverse incidents during the transport of patients with IMD at paediatric age?

D - In patients with suspected or confirmed diagnosis of IMD who require resuscitation and transfer to an ICU, it is recommended to inform the hospital or destination unit.

D - It is recommended that specialized transport units perform the transfer of patients with suspected or confirmed diagnosis of IMD to a reference centre.

Management of IMD in the ICU

Considerations Before Admission to an ICU

Questions to Answer

- In patients with IMD requiring admission to the ICU, is there evidence that the time delays in consultation at a specialist centre or paediatric ICU affect the results (mortality and residual disability)?
- In patients with IMD requiring admission to the ICU, is there any evidence that the following factors affect the results?
  - Stabilization and transport by a specialized paediatric team
  - Paediatric intensive care
  - Remote telephone support
  - Early referral and/or recovery (or quick resolution of the process)

D - Patients who arrive at the hospital emergency unit with suspected IMD should be examined and treated immediately by an experienced physician, preferably a paediatric specialist.

D - In patients with clinical progression of IMD, it is advisable to contact the ICU in the early stages.

Supportive Therapy in the ICU

Question to Answer

- In patients requiring intensive care, is there evidence that the following interventions influence mortality and morbidity?
  - Ventilation/airway management
  - Catecholamines
  - Invasive monitoring
  - Haemofiltration, continuous venovenous haemofiltration, plasmapheresis
  - ECMO (extracorporeal membrane oxygenation)
  - Mechanical circulatory support (hyperosmolar fluids)
  - Plasmafiltration
  - Corticosteroids, high-dose or physiological replacement
  - Invasive management of intracranial hypertension

D - Catecholamines are recommended at an early stage to manage patients with fluid resistant meningococcal septic shock and the support with mechanical ventilation should be considered for these patients.

GCP - In patients with meningococcal septic shock resistant to catecholamine, intravenous terlipressin and titrated doses of corticosteroids are considered proper rescue measures.

D - Paediatric patients with meningococcal septic shock resistant to catecholamines could benefit from the use of terlipressin as a rescue therapy.

D - Non-invasive monitoring (electrocardiogram [ECG], blood pressure, temperature, oxygen saturation) of patients with fluid sensitive meningococcal septic shock is recommended. A central access (arterial or venous) will be channelled in cases of fluid resistant meningococcal septic.

GCP - Patients with acute respiratory distress syndrome secondary to IMD who do not respond to standard therapy may benefit from extracorporeal membrane oxygenation.

GCP - Patients with fluid resistant meningococcal septic shock, severe metabolic acidosis, acute or impending renal failure, and complex or problematic fluid balance, may benefit from continuous veno-venous haemofiltration.

Adjuvant Therapies

Question to Answer

- In patients with IMD in the ICU, is there any evidence that the following haematologic and immunologic measures reduce mortality and morbidity?

- Activated protein C and protein C
- Immunoglobulins
- Heparin
- FFP
- PGI2 (prostacyclin)
- Tissue plasminogen activator (t-Pa) antagonists of the platelet activating factor (PAF) antithrombin III

A - The administration of activated protein C or recombinant bactericidal permeability increasing protein is not recommended for paediatric patients with severe IMD.

A - In case of severe sepsis, the use of an intravenous immunoglobulin treatment is not taken into consideration.

Surgical Management of IMD

Questions to Answer

- In patients with extensive skin affection, do compartment pressure control and fasciotomy reduce the number and extension of tissue necrosis, amputations and degree of residual disability?
- In patients with IMD and complications, what is more effective and safe to reduce tissue necrosis or prevent amputation or secondary infection: early surgical debridement or the conservative treatment?

D - Monitoring of compartmental pressure in patients with IMD and extensive vascular involvement of a limb should be considered.

GCP - It is necessary to resort to a specialist urgently to assess and interpret the monitoring of compartmental pressure.

D - Urgent debridement is recommended if secondary infections of the wound appear in the paediatric patient, if the situation allows.

GCP - From the early hours of admission, orthopaedic and plastic surgeons should be consulted to assess the patient's needs.

GCP - The need in some cases to amputate large body areas poses an ethical conflict that should be discussed jointly by surgeons and intensive care physicians, taking into account the views of parents or caregivers.

GCP - In patients with meningococcal purpura fulminans and ischemia, the possibility of performing the arthrolysis technique when the human and technical resources are available should be considered.

Prognostic and Severity Factors of IMD

Clinical Factors as Severity Indicators

Question to Answer

- In patients with suspected IMD, what clinical factors are useful to predict survival, mortality or sequelae?
  - Clinical signs: tachycardia, tachypnoea, hypotension, poor peripheral perfusion, central and peripheral temperature difference, severity or extent of the eruption, eruption progression, presence of fever, stiff neck, irritability or nervousness, lethargy, fatigue, drowsiness, level of consciousness
  - Laboratory study: white blood cell count, coagulopathy, CRP, platelets, blood gases, kidney function, liver function, cortisol, glucose, other (creatine phosphokinase [CPK], rhabdomyolysis)

C - It should be taken into account that the following factors are associated with high mortality in paediatric patients with IMD:

- A product of the platelet and neutrophil count $<40 \times 10^9/l$
- A procalcitonin level >150 ng/ml

C - It should be taken into account that the presence of leukopenia ($<4,500$ cells/mm^3) is a factor associated with an unfavourable clinical evolution in paediatric patients with IMD.

C - It should be taken into account that the following factors are associated with extreme severity in paediatric patients with IMD:

- Evolution of symptoms in less than 24 hours
- Presence of a number of petechiae over 50
- Decreased level of consciousness

- Presence of shock

D - It should be taken into account that meningococcal meningitis carries less risk of unfavourable neurological evolution than the meningitis caused by other bacteria.

Severity and Mortality Risk Scoring Systems

Question to Answer

- In patients with suspected IMD, is there any evidence that the use of any of the following prognostic scales can predict the severity of the disease or the risk of poor clinical results?
    - Leclerc
    - *Glasgow Meningococcal Septicaemia Prognostic Score* (GMSPS)
    - Gedde-Dahl's MOC score

GCP - In patients with suspected or confirmed diagnosis of IMD, a rating scale will be used to identify changes in the patient's condition.

B - For patients with suspected or confirmed diagnosis of IMD, the GMSPS scale can be a good tool for identifying changes in the patient's health condition.

GCP - If a patient with suspected or confirmed diagnosis of IMD shows a worsening of his/her health condition, the ICU will be contacted immediately.

Prevention and Control of IMD

Indications for Antibiotic Prophylaxis

Question to Answer

- What evidence is there that the following groups, after having had contact with a patient with IMD in the past seven days, should receive antibiotic prophylaxis?
    - People who have had contact within the household
    - Students from the same class or school
    - People who have had contact with body fluids (after resuscitation)
    - People who have exchanged kisses
    - People who have shared drinks
    - People who have shared any means of transportation

D - Chemoprophylaxis is recommended as soon as possible, preferably in the first 24 hours, for all those who have had close contact (see glossary) and prolonged exposure to a case of IMD in the family (living or sleeping in the same house) or in a comparable context (shared kitchen within a student residence, shared apartment, etc.) during the 7 days before the onset of symptoms in the case.

D - In preschoolers (up to 6 years), the administration of chemoprophylaxis is recommended to all the students who attend the same classroom as the sporadic case as well as the classroom staff. Chemoprophylaxis is not indicated for the students and staff of other classes from the same school other than the IMD case.

D - It is not recommended to administer chemoprophylaxis for students attending the same class or the same primary, secondary school and university as a sporadic case, unless the case is in close contact with the rest.

D - Chemoprophylaxis should be offered to all health care workers whose mouth or nose may have been exposed to respiratory secretions from a patient with IMD before the patient has completed the first 24 hours of antibiotic therapy.

GCP - The following situations are not, by themselves, indicative of chemoprophylaxis:

- Sharing drinks, food, cigarettes or kissing on the cheek, or other acts involving a similar contact with saliva
- Sharing occasionally the same transport vehicle, even if it is occupying the seat next to the case of IMD

Antibiotics of Choice for the Prophylaxis of IMD

Questions to Answer

- What evidence is there that the following antibiotics are effective for the prevention of IMD in contact groups?
  - Rifampicin
  - Ciprofloxacin
  - Ceftriaxone
- In people who have maintained close contact with a case of IMD, what is more effective in preventing secondary cases: oral rifampicin or intramuscular ceftriaxone?
- In people who have maintained close contact with a case of IMD, what is more effective in preventing secondary cases: oral rifampicin or oral ciprofloxacin?

GCP - Post-exposure chemoprophylaxis with rifampicin is recommended as first choice. The administration of ceftriaxone is recommended as an alternative in the following circumstances:

- When rifampicin is contraindicated (see info: http://www.aemps.gob.es/)
- If there is alcohol consumption and malnutrition, when it is considered that the risk exceeds the potential benefit for the patient
- In contacts <18 years, when a new intervention is required in the context of an outbreak and the previous prophylaxis had been performed with rifampicin
- When suspecting a possible breach of the oral chemoprophylaxis

And the administration of ciprofloxacin as an alternative to rifampicin in the following circumstances:

- In contacts >18 years, when a new intervention is required in the context of an outbreak and the previous prophylaxis had been performed with rifampicin.

Meningococcal Vaccination of Patients with IMD

Question to Answer

- Can the meningococcal vaccination of cases of IMD reduce the risk of a second IMD when compared to patients who have been diagnosed and treated by IMD and have not been vaccinated?

D - It is recommended to provide monovalent conjugate vaccine against *Neisseria meningitidis* serogroup C (MenC) before hospital discharge after having suffered from IMD to the following groups:

- Patients with confirmed IMD by serogroup C who have previously been immunized with MenC
- All patients not previously immunized with MenC, regardless of the serogroup, causing the episode

Other Infection Control Measures

Question to Answer

- In patients with suspected IMD, are measures such as the isolation in an individual room, the use of individual protection equipment (non-sterile clean gloves, non-sterile clean gown, waterproof mask, eye or facial protector) and chemoprophylaxis, effective in hospital care to reduce the risk of secondary infection associated to health care by clinical staff (except laboratory staff), family or people living with the index case?

D - Paediatric patients with suspected IMD should be initially admitted to a single room.

D - When a suspected case of IMD is admitted to hospital, droplet transmission precautions should be taken, which can be interrupted after 24 hours of effective treatment of the patient.

D - Health care staff at high risk of exposure to respiratory secretions must use appropriate individual protective equipment.

Follow-up after IMD

Sequelae Associated to IMD and Support to Patients, Family and Caregivers

Questions to Answer

- What are the sequelae associated to IMD and what aspects need greater support and information for patients and their families and caregivers?
- What proportion of the paediatric population with bacterial meningitis develops physical or psychological morbidity?

- What proportion of the paediatric population with meningococcal septicaemia develops physical or psychological morbidity?

GCP - The patient who has suffered IMD must leave the hospital with an individualized care plan.

GCP - The individualized care plan for patients who have suffered IMD shall describe the monitoring to be performed in order to identify immediate complications that may occur in the long term. Furthermore, the individualized care plan shall include an extensive list of professionals, schools, associations, foundations and institutions that can help the patient affected and his/her families to manage their new life, not forgetting to include those public or private institutions, which can provide financial assistance.

GCP - The patient who has suffered from IMD and their families should be informed of the following potential long-term consequences:

- Hearing loss
- Orthopaedic sequelae (damage to bones or joints)
- Skin lesions (scarring from necrosis)
- Psychosocial issues
- Neurological and developmental disorders
- Renal failure

They should be informed of the characteristics of the disease, its prevalence, case fatality, morbidity, and the usual means of transmission, etc., to try to minimize the guilt that usually appears in all those people closely involved with the patient.

The individualized care plan shall include delivery to the family of a free printed copy of this clinical practice guideline (CPG) in its version for patients, families and caregivers.

GCP - Hearing and neurologic tests should be performed to any patient who has suffered IMD, in order to establish a treatment as soon as possible if necessary.

D - Before discharge, the family should be offered the possibility to acquire the appropriate skills to engage with the basic care of the paediatric patient.

D - When the patient is far from the hospital, the opportunity to acquire skills related to specialized care should be offered.

D - Providing the family with psychological support will help them to decide and mitigate the intensity of posttraumatic stress disorder (PTSD) if it appears.

GCP - Health care professionals should be offered the means to enable them to acquire effective communication skills.

Impact on Families and Caregivers

Question to Answer

- Do families and caregivers of those who have suffered IMD suffer any psychosocial problems? And, if so, do the psychosocial interventions and supply of information improve their quality of life?

C - Health care professionals involved in the monitoring of paediatric patients with IMD should be aware of the possibility of PTSD with anxiety or depression in patients, their families and caregivers.

B - It is recommended that a psychologist or psychotherapist monitors in the short-term (up to 2 years) patients with IMD and their parents in the weeks following the discharge from the paediatric ICU, or if the patient dies, in order to reduce the scope of the psychological sequelae of the disease.

Awareness and Information Campaigns on IMD

Question to Answer

- Do the educational programs aimed at health professionals and the population in general improve the speed of recognition, diagnosis, and treatment of IMD? Do they increase survival or decrease the severity of the disease and its complications? Do they have any effect on the admission to the ICU or the duration of hospital stay, admission costs, the duration of school absence, etc.?

GCP - The general population and other groups (such as pharmaceuticals, day carers, etc.) should be informed about IMD in order to suspect the disease at an early stage.

GCP - The general population should know the implications of the appearance of petechiae for early detection of the IMD.

Definitions

Scottish Intercollegiate Guidelines Network (SIGN) Levels of Evidence for Intervention Studies

1++	High quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of clinical trials or well-conducted clinical trials with low risk of bias
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with a high risk of bias
2++	High quality systematic reviews with cohort or case-control studies; Cohort or case-control studies with very low risk of bias and a high probability of establishing a causal relationship
2+	Well-conducted cohort or case-control well conducted studies with low risk of bias and a moderate probability of establishing a causal relationship
2-	Cohort or case-control studies with high risk of bias and a significant risk that the relationship is not causal
3	Non-analytic studies, such as case reports and case series
4	Expert opinion

Note: Studies classified as 1- and 2- should not be used for making recommendations due to their high potential for bias.

Levels of Evidence for Diagnostic Questions

Levels of Scientific Evidence	**Type of Evidence**
Ia	Systematic review with homogeneity of level 1 studies
Ib	Level 1 studies
II	Level 2 studies Systematic review of studies rated as 2
III	Level 3 studies Systematic review of studies of level 3
IV	Consensus, expert opinions without explicit critical appraisal
Level 1 Studies	Meet the following requirements: • Blinded comparison with a valid reference test ("gold standard") • Adequate spectrum of patients
Level 2 Studies	They have only one of these biases: • Unrepresentative population (the sample does not reflect the population to which the test applies) • Comparison with the inadequate reference standard ("gold standard") (the test being evaluated as part of the gold standard or the test result affects the implementation of the gold standard) • Unblinded comparison • Case-control
Level 3 Studies	They have two or more of the criteria described in level 2 studies

Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendation for Intervention Studies

A	At least one meta-analysis, systematic review or clinical trial rated as 1++ and directly applicable to the target population of the guide, or a body of evidence including studies rated as 1+ and good agreement between them
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating the good agreement between them, or extrapolated scientific evidence from studies rated as 1++ or 1+

C	A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results, or extrapolated scientific evidence from studies rated as 2++
D	Scientific evidence levels 3 or 4, or extrapolated scientific evidence from studies rated as 2+
Q	Evidence obtained from relevant and high quality studies. This category is not contemplated by the Scottish Intercollegiate Guidelines Network (SIGN).
Good Clinical Practice (GCP)*	Recommended practice based on clinical experience and consensus of the development group

*Sometimes the development group realizes some important practical aspect which may want to be emphasized and for which there is probably no supporting evidence. In general, these cases have to do with some aspect of the treatment considered good clinical practice (GCP) and that no one would normally question. These aspects are considered GCP points. These messages are not an alternative to evidence-based recommendations, but should be considered only when there is no other way to highlight this aspect.

Grades of Recommendation for Diagnostic Questions

Recommendation	Evidence
A	Ia or Ib
B	II
C	III
D	IV

Clinical Algorithm(s)

The following clinical algorithms are included in the original guideline document:

- Algorithm 1: Signs and symptoms of IMD
- Algorithm 2: Pre-hospital management of IMD
- Algorithm 3: Hospital Management of IMD
- Algorithm 4: Hospital management of meningococcal meningitis

Scope

Disease/Condition(s)

Invasive meningococcal disease (IMD)

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Critical Care

Family Practice

Infectious Diseases

Internal Medicine

Neurology

Pediatrics

Preventive Medicine

Surgery

Intended Users

Advanced Practice Nurses

Emergency Medical Technicians/Paramedics

Hospitals

Nurses

Patients

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Social Workers

Guideline Objective(s)

- To provide health care professionals who work in the field of primary and hospital care with a set of recommendations for the clinical management of the invasive meningococcal disease (IMD) based on the best scientific evidence available
- To optimize the clinical management of the IMD among the young population, with recommendations aimed at achieving early detection and rapid initiation of the treatment to reduce the high morbidity and mortality associated with the disease

Target Population

Patients aged between one month and 19 years suspected of having invasive meningococcal disease (IMD) or with confirmed IMD and their contacts

Note: Some questions addressed in this clinical practice guideline (CPG) have focused exclusively on paediatric population. It does not include infants less than one month because the aetiology and pathogenesis of meningitis and sepsis during this age period is different.

Interventions and Practices Considered

Diagnosis/Evaluation

1. Recognition of warning signs and symptoms or red flags
2. Clinical reassessment as strategy to improve diagnosis

3. Non-specific laboratory tests
4. Diagnosis of increased intracranial pressure
5. Microbiological confirmation tests

Treatment/Management/Prevention

1. Pre-hospital management
    - Pre-hospital administration of antibiotics
    - Pre-hospital resuscitation
    - Development and implementation of protocols
2. Hospital management
    - Antibiotic treatment (ceftriaxone, cefotaxime)
    - Sampling for microbiological diagnosis
    - Indications for lumbar puncture
    - Early supportive therapy (corticosteroids, intravenous fluids, respiratory and circulatory support)
    - Stabilization and transport to a paediatric intensive care unit (ICU)
3. Management in the ICU
    - Considerations before admission to an ICU
    - Supportive therapy in the ICU (catecholamines, invasive monitoring, haemofiltration, extracorporeal membrane oxygenation [ECMO])
    - Adjuvant therapies (coagulation, immunomodulators)
    - Surgical management
4. Assessment of prognostic and severity factors of invasive meningococcal disease (IMD)
    - Use of clinical factors as severity indicators
    - Use of severity and mortality risk scoring systems
5. Prevention and control of IMD
    - Indications for antibiotic prophylaxis
    - Antibiotics of choice for the prophylaxis of IMD
    - Meningococcal vaccination of patients with IMD
    - Other infection control measures
6. Follow-up after IMD
    - Follow-up of sequelae associated with IMD (e.g., hearing loss, orthopaedic complications, cutaneous complications, psychosocial and psychiatric complications, neurological complications)
    - Providing support to patients, family, and caregivers
7. Awareness and information campaigns on IMD

Major Outcomes Considered

- Sensitivity, specificity, positive/negative predictive value of diagnostic tools
- Morbidity
- Mortality
- Quality of life
- Survival rate
- Overall incidence rate
- Neurological sequelae

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

The creation and selection of the clinical questions was conducted based on questions that address controversial issues in other guides, that is, questions which require a thorough review by the Guideline Development Group (GDG) to identify the latest advances in materials, as well as questions that have arisen within the GDG itself, until a total of thirty-eight questions related to epidemiology, diagnosis, treatment, prevention and monitoring of invasive meningococcal disease (IMD) among the population described. The development of the clinical questions was conducted considering the PICO (Patient/Intervention/Comparison/Outcome) format.

The next step was to conduct an initial literature search in databases and other specialized sources (Medline, EMBASE, Excelencia Clínica, Trip Database, GuíaSalud, National Guideline Clearinghouse (NGC), Guidelines International Network-GIN), in order to locate other clinical practice guidelines (CPGs), national or international, dealing with similar topics.

This search resulted in the location of five guides, two of which were discarded because the population, topics, interventions, completion date or methodology did not meet the aims and scope of this CPG. The three remaining guides were evaluated, using the AGREE instrument (Appraisal of Guidelines Research and Evaluation). All of them met the minimum requirement previously established to be a source of evidence in this guide: achieving a score above 65% in terms of rigour of development.

Two guides have become secondary sources of evidence to answer several clinical questions, and it is indicated so in the different sections of this document where the conclusions or studies extracted from them have been set out. To adapt and update the evidence from the above guidelines, the methodology proposed by Osteba in its "Informe de Evaluación sobre Descripción de la Metodología empleada en la GPC sobre Asma" was used. The guide of the European Centre for Disease Prevention and Control (ECDC) focuses exclusively on the chemoprophylaxis of the contacts of patients with IMD.

For the nineteen clinical questions addressed in this guide, which the CPG Scottish Intercollegiate Guidelines Network (SIGN) already included, searches from 2006 until 2011, during the months between April and August, were carried out to update and adapt those used by SIGN. Likewise, for the thirteen questions already collected by the CPG National Institute for Health and Care Excellence (NICE), these were updated with the searches from 2009 until 2011, during the months between April and August, adapting them to those used by NICE. For the six remaining questions, new specific search strategies were developed to expand the search period without a limiting date. Additionally, automatic email alerts were defined for new articles added to Medline (PubMed).

The search strategies were conducted combining terms in controlled language within each database (MeSH, Emtree, and Decs) and free language, in order to improve and balance their sensitivity and specificity. The sources were Medline (PubMed), EMBASE (Elsevier.com), Centre for Reviews and Dissemination (CRD) Databases, Cochrane Library, Índice Bibliográfico Español en Ciencias de la Salud (IBECs) and Latin American and Caribbean Literature on Health Sciences (LILACs).

The searches were based on the most appropriate types of studies in relation to the characteristics of each question and the following languages: Spanish, French, English, Catalan, Italian and Portuguese.

A reverse search of the references of articles identified and included in this guide was carried out. Grey literature was also searched in a non-systematic way.

The search results were peer reviewed; the clinical guide coordinator resolved any discrepancy situations. Initially, screening was done by title and abstract. In a second screening, studies were discarded and the causes of exclusion identified.

The inclusion and exclusion criteria were:

1. Population aged between one month and 19 years suspected of having IMD or with confirmed IMD and their contacts. Some questions addressed in this CPG have focused exclusively on paediatric population.
2. Infants aged less than one month were excluded because the aetiology and pathogenesis of meningitis and sepsis during this age period are different.

Included in the Methodological Material document is a description of the methodology for each question, with a description of the search strategy (information sources, limits, identified studies, included studies, bibliographic searches).

Number of Source Documents

Refer to the Methodological Material document for a breakdown of the identified studies and included studies for each clinical question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Scottish Intercollegiate Guidelines Network (SIGN) Levels of Evidence for Intervention Studies

1++	High quality meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of clinical trials or well-conducted clinical trials with low risk of bias
1-	Meta-analyses, systematic reviews of clinical trials or clinical trials with a high risk of bias
2++	High quality systematic reviews with cohort or case-control studies; Cohort or case-control studies with very low risk of bias and a high probability of establishing a causal relationship
2+	Well-conducted cohort or case-control well conducted studies with low risk of bias and a moderate probability of establishing a causal relationship
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3	Non-analytic studies, such as case reports and case series
4	Expert opinion

Note: Studies classified as 1- and 2- should not be used for making recommendations due to their high potential for bias.

Levels of Evidence for Diagnostic Questions

Levels of Scientific Evidence	Type of Evidence
Ia	Systematic review with homogeneity of level 1 studies
Ib	Level 1 studies
II	Level 2 studies Systematic review of studies rated as 2
III	Level 3 studies Systematic review of studies of level 3
IV	Consensus, expert opinions without explicit critical appraisal
Level 1 Studies	Meet the following requirements: • Blinded comparison with a valid reference test ("gold standard") • Adequate spectrum of patients
Level 2 Studies	They have only one of these biases: • Unrepresentative population (the sample does not reflect the population to which the test applies) • Comparison with the inadequate reference standard ("gold standard") (the test being evaluated as part of the gold standard or the test result affects the implementation of the gold standard) • Unblinded comparison • Case-control studies
Level 3 Studies	They have two or more of the criteria described in level 2 studies

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The selected studies were evaluated by means of the critical reading tool of the Agency for Health Technology Assessment of the Basque Country - OSTEBA. These studies were classified according to the evidence levels proposed by the Scottish Intercollegiate Guidelines Network (SIGN) for intervention studies and according to the adjustment of the levels of evidence of the Centre for Evidence-Based Medicine in Oxford, proposed by the National Institute for Health and Care Excellence (NICE) for Diagnostic test studies (see the "Rating Scheme for the Strength of the Evidence" field).

The detailed information on the methodology applied to the clinical practice guideline (CPG) (search strategies for each clinical question and tables summarizing the evidence and formal evaluation) are available from GuíaSalud Web site (see also the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The methodology used in the preparation of this clinical practice guideline (CPG) is set out in the *Methodology Manual for Preparation of CPG in the NHS*.

The development of this CPG began with the establishment of the Guideline Development Group (GDG), composed of 12 clinicians from diverse health fields: primary and hospital care, and other specialties such as nursing, paediatrics, internal medicine, family and community medicine, paediatric intensive medicine, microbiology, orthopaedics and preventive medicine and public health. Moreover, from the early stages a group of citizens supported by the Irene Megías Foundation against meningitis took part. There were also four additional citizens to review the information for patients, families and caregivers. The review focused on the understandability of the content and identifying the information that they felt should be included in the document.

The critical reading tool from the Agency for Health Technology Assessment of the Basque Country - OSTEBA simplifies the synthesis work of the literature, which, following a review by the GDG, served as material for any development of the recommendations through formal assessment or reasoned judgment. In addition to the volume and quality of evidence, the GDG should consider the applicability of the findings, the correlation of the data and the relevance of its application in our National Health System or its clinical impact. For those clinical questions for which the volume of evidence turned out to be little or none, poor methodological quality (level of evidence 1- and 2-) or inconsistent, recommendations were made based on the consensus of the group that had taken into account, as well as additional factors, others such as routine clinical practice, the availability of intervention in the environment, the benefit-risk ratio or even the data sheet of the drug.

Rating Scheme for the Strength of the Recommendations

Scottish Intercollegiate Guidelines Network (SIGN) Grades of Recommendation for Intervention Studies

A	At least one meta-analysis, systematic review or clinical trial rated as 1++ and directly applicable to the target population of the guide, or a body of evidence including studies rated as 1+ and good agreement between them
B	A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating the good agreement between them, or extrapolated scientific evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results, or extrapolated scientific evidence from studies rated as 2++
D	Scientific evidence levels 3 or 4, or extrapolated scientific evidence from studies rated as 2+

Q	Evidence obtained from relevant and high quality studies. This category is not contemplated by the Scottish Intercollegiate Guidelines Network (SIGN)
Good Clinical Practice (GCP)*	Recommended practice based on clinical experience and consensus of the development group

*Sometimes the development group realizes some important practical aspect which may want to be emphasized and for which there is probably no supporting evidence. In general, these cases have to do with some aspect of the treatment considered good clinical practice and that no one would normally question. These aspects are considered good clinical practice points. These messages are not an alternative to evidence-based recommendations, but should be considered only when there is no other way to highlight this aspect.

Grades of Recommendation for Diagnostic Questions

Recommendation	Evidence
A	Ia or Ib
B	II
C	III
D	IV

Cost Analysis

- The developers of the National Institute for Health and Care Excellence (NICE) clinical practice guideline (CPG) performed a study on cost-effectiveness (for suspected bacterial meningitis or invasive meningococcal disease [IMD]) by comparing penicillin, cefotaxime and ceftriaxone, and concluded that for patients weighing 37 kg or less, ceftriaxone was the cheapest option; for patients between 37 kg and 51 kg, penicillin and ceftriaxone had similar costs and, for patients weighing more than 51 kg, the administration of penicillin was the cheapest option. They found that, for patients weighing 30 kg or less, penicillin was the most expensive option. Cefotaxime is the antibiotic most used in our environment; according to the NICE CPG an option with an average cost when compared to penicillin and ceftriaxone.
- The development group of the NICE CPG also carried out a cost-effectiveness study of crystalloid vs. colloid resuscitation fluids. The colloid solution was considerably more expensive (£34) than the crystalloid solution (£0.51). The crystalloid solution is considered more cost-effective than the colloid solution.
- In 2005, the Fundación Hospital Son Llàtzer designed a computer protocol on integrated management of sepsis (PIMIS) in adults. Its implementation has resulted in a decrease in both hospital mortality in severe sepsis (11.4%) and septic shock (5.4%), and in a clear decrease in the length of hospital stays and economic cost associated.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Following the completion of a first draft, the text was submitted to a peer review process in two parts: one focused solely on the recommendations, carried out by expert contributors, and another part of comprehensive review conducted by external reviewers. The expert contributors and the external reviewers in most cases have been nominated by their respective scientific societies. The reviewers completed a standard form with two different sections. The first consisted of closed questions aimed at knowing the general opinion on the draft of the guide and evaluate its applicability. The second consisted of sections for each chapter of the guide in which free text was included. One participant made a partial revision (one chapter). The comments and suggestions of reviewers and contributors were referred to the Guideline Development Group (GDG) for evaluation after being subjected to an initial screening (in terms of form and style). The external review resulted in the development of two new recommendations and the introduction of minor changes in 8 recommendations aimed at changing their scope.

The clinical practice guideline (CPG) underwent a Public Exposure process, in which the draft of the CPG was revised by other organizations in the field of health, previously registered and interested in contributing to it. In the case of this CPG four organizations were involved, whose

contributions and comments are available for viewing on the GuíaSalud Web site .

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Early diagnosis and immediate initiation of appropriate treatment greatly improves prognosis and the quality of life of patients. Appropriateness of care at every stage of the disease (acute, moderate and sequelae) is critical to achieve a favourable outcome. Also in the case of children and adolescents, the impact of hospitalization, treatment, sequelae and deaths, is greater not only for the patients themselves, also for family members and caregivers.

Potential Harms

- Pre-hospital administration of antibiotics in patients with suspected invasive meningococcal disease (IMD) could delay transport to the hospital and even be the cause of a definitive diagnosis masking. It is a fact that IMD usually progresses rapidly and there is the belief that early administration of an active antibiotic against *Neisseria meningitidis* would affect the reduction of morbidity and mortality. By contrast, it has been suggested that early administration of antibiotics in an environment outside the hospital would cause initial worsening of the IMD due to the bacterial lysis they induce and it would be safer to administer it in hospital.
- Adverse effects of intravenous administration of dexamethasone or methylprednisolone include gastrointestinal bleeding, herpes zoster, herpes simplex, fungal infections or high fever.
- The administration of hydrocortisone was associated with an increased risk of new episodes of sepsis or septic shock.
- The optimal volume of fluid to be administered as initial therapy in paediatric patients with bacterial meningitis is unknown. In environments with high mortality and delayed access to health care, fluid restriction appears to increase the risk of neurological sequelae.
- Transportation is a period of high risk and problems can occur, such as endotracheal tube obstruction, loss of venous line or secondary hemodynamic destabilization to movement. It is therefore essential that the transfer is performed by specific paediatric trained staff.
- Terlipressin is a potentially valid alternative rescue treatment for catecholamine-resistant septic shock in paediatric patients. It must be considered that, when associated with high doses of catecholamines, it entails the risk of excessive vasoconstriction and ischemia.
- The administration of ceftriaxone as prophylaxis of IMD increases the risk of nasopharyngeal de novo colonization with respect to rifampicin by 4% after 6 days and 1.5% after 14 days.

Contraindications

Contraindications

- Contraindications to lumbar puncture:
  - Clinical or radiological signs of increased intracranial pressure
  - Shock
  - After convulsions, until stabilization of the patient
  - Coagulation abnormalities:
    - Coagulation tests (if performed) outside the normal range
    - Platelet count <100 x 10^9/L
    - On anticoagulant treatment

    - Local infection at the lumbar puncture site
    - Acute respiratory failure
- The occurrence of bleeding diathesis would contraindicate surgical management of invasive meningococcal disease (IMD) because of the risk of bleeding, according to some authors.
- Rifampicin is contraindicated in pregnant women, during lactation, for cases of alcoholism and liver disease.
- The data sheet for ciprofloxacin contraindicates its use in paediatric patients because it causes arthropathy in juvenile animals.

Qualifying Statements

Qualifying Statements

This clinical practice guideline (CPG) is an aid to decision making in health care. The compliance of this guide is not mandatory, nor does it replace the clinical judgement of the health care personnel.

Implementation of the Guideline

Description of Implementation Strategy

This clinical practice guideline (CPG) is a helpful tool for professionals and users in making decisions on the most appropriate health care. It is therefore necessary to introduce and implement the recommendations of this guideline in those areas of the health care environment in which its application is relevant. The following strategies are recommended for these to be performed appropriately:

- Presentation of the CPG to the media by the health authorities
- Presentation of the CPG to the various national associations and societies of paediatrics, family medicine, accident and emergency medicine, internal medicine, preventive medicine, microbiology and paediatric intensive care
- Presentation of the CPG to the relevant regional associations
- Distribution of the abridged version to various institutions and organizations in the health care environment
- Collaboration with the scientific societies that have participated in the review of the CPG, to promote its dissemination
- Sending and distribution of this CPG to different CPG collector databases, for their evaluation and inclusion in them
- Free access to the different versions of the CPG on the GuíaSalud Web site
- Dissemination and information on the CPG in scientific activities related to paediatrics, family medicine, accident and emergency medicine, internal medicine, preventive medicine, microbiology and paediatric intensive care
- Translation of the full version into English

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Working Group of the Clinical Practice Guideline on the Management of Invasive Meningococcal Disease. Clinical practice guideline on the management of invasive meningococcal disease. Madrid (Spain): Ministry of Health, Social Services and Equality; Aragon Institute for Health Sciences; 2013. 173 p. (Clinical Practice Guidelines in the NHS: IACS; no. 2011/01). [134 references]

Adaptation

Not applicable: The guideline is not adapted from another source.

Date Released

2013

Guideline Developer(s)

Aragon Institute for Health Sciences - State/Local Government Agency [Non-U.S.]

GuiaSalud - National Government Agency [Non-U.S.]

Ministry of Health (Spain) - National Government Agency [Non-U.S.]

Guideline Developer Comment

Cooperating Societies:

- Spanish Association of Paediatrics
- Spanish Association of Primary Care Paediatrics
- Irene Megías Foundation against Meningitis
- Spanish Society of Clinical Microbiology and Infectious Diseases
- Spanish Society of Epidemiology
- Spanish Society of Community Pharmacy
- Spanish Society of Paediatric Infectious Diseases
- Spanish Society of Family and Community Medicine
- Spanish Society of Paediatric Neurology
- Spanish Society of Paediatric Emergency

The members of these societies have participated in the creation, expert collaboration, and external review of this clinical practice guideline (CPG).

Source(s) of Funding

This clinical practice guideline (CPG) has been produced under the collaborative agreement signed by the Carlos III Health Institute, an autonomous council of the Ministry of Economy and Competitiveness and the Aragon Institute for Health Sciences (IACS), in the framework of developing activities of the Spanish Network of Agencies for Health Technology Assessment and NHS benefits, financed by the Ministry of Health, Social Services and Equality.

Guideline Committee

Working Group of the Clinical Practice Guideline on the Management of Invasive Meningococcal Disease

Composition of Group That Authored the Guideline

Working Group of the Clinical Practice Guideline on the Management of Invasive Meningococcal Disease

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Financial Disclosures/Conflicts of Interest

All members of the Working Group, as well as those who have participated in the expert collaboration and external review, have made the declaration of interest as appears in Appendix 4 in the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available in English and Spanish from the GuíaSalud Web site.

Availability of Companion Documents

The following are available:

- Quick reference guides and summary versions are available from the GuíaSalud Web site.
- The Spanish version of the guideline is also available via a mobile application from the GuíaSalud Web site.
- Working Group for CPG Updates. Updating clinical practice guidelines in the National Health System: methodology handbook. Madrid (Spain): National Health System Quality Plan of the Spanish Ministry of Health and Social Policy; Aragon Institute for Health Sciences (IACS); 2009. 67 p. (Clinical Practice Guidelines in the National Health System: IACS; no. 2007/02-01). Available from the GuíaSalud Web site.

Patient Resources

Patient information can be found in Appendix 1 of the original guideline document. A Spanish version is also available from the GuíaSalud Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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